

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Re: Appeal to the Board of Patent Appeals and Interferences

Appellants: Vance, et al.)	Examiner: Vinod Kumar
)	
Serial Number: 10/623,930)	Group Art Unit: 1638
)	
Filed: July 21, 2003)	Customer Number: 22827
)	
Confirmation No.: 6465)	Deposit Account: 04-1403
)	
Title: Compositions and Methods for the Modulation of Gene Expression in Plants)	Attorney Docket No. USC-164
)	

1. ☐ **NOTICE OF APPEAL:** Pursuant to 37 CFR 41.31, Applicant hereby appeals to the Board of Appeals and interferences from the last decision of the Examiner.
2. ☐ **PRE-APPEAL BRIEF REQUEST FOR REVIEW:** Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request. This request is being filed with a Notice of Appeal. The review is requested for the reason(s) stated on the attached sheet(s) [No more than five (5) pages may be provided.]
3. ☐ **BRIEF** on appeal in this application pursuant to 37 CFR 41.37 is transmitted herewith (1 copy).
4. ☐ An **ORAL HEARING** is respectfully requested under 37 CFR 41.47 (due within two months after Examiner's Answer).
5. ☒ Reply Brief under 37 CFR 41.41(b) is transmitted herewith (1 copy).
6. ☐ "Small entity" verified statement filed: [] herewith [] previously.

7. FEE CALCULATION:

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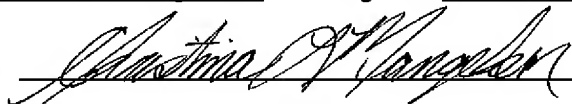
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Date: June 16, 2010

I hereby certify that this correspondence and all attachments and any fee(s) are being electronically transmitted via the internet to the U.S. Patent and Trademark Office using the Electronic Patent Filing System on June 16, 2010.

Suzanne Haynes

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(Signature of person transmitting documents)

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Plants)	

REPLY BRIEF

In response to the Examiner's Answer dated April 16, 2010, please refer to the following remarks:

Status of the Claims beginning on page 2.

Grounds of rejection to be reviewed on Appeal beginning on page 3.

Arguments beginning on page 4.

STATUS OF CLAIMS

Currently, claims 1-5, 20, 23, and 26 remaining pending including independent claims 1, 20, and 23. Claims 6-19, 21-22, and 24-25 have been previously cancelled from the application. Claims 1-5 stand withdrawn as directed to non-elected inventions. All pending claims are attached hereto in the Claims Appendix.

In the Office Action of June 2, 2009, claims 20, 23, and 26 were rejected.

The rejection of claims 20, 23, and 26 has been appealed.

GROUND OF REJECTION TO BE REVIEWED ON APPEAL

Claims 20, 23, and 26 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Cullen, et al. (U.S. Published Patent Application No. 2004/0053411, claiming filing benefit of U.S. Provisional Patent Application 60/337,224 having a filing date of May 3, 2002) in view of Llave, et al. (*The Plant Cell*, **14**:1605-1619, 2002) and Reinhart, et al. (*Genes & Development*, **16**:1616-1626, 2002).

ARGUMENT

In the Examiner's Answer, reference is made throughout to U.S. Published Patent Application 2004/0053411 to Cullen, et al. As discussed in the Appeal Brief, this published application is not proper prior art under 35 U.S.C. §102 to the pending claims of the captioned application. The captioned application properly claims filing benefit under 35 U.S.C. §120 to U.S. Provisional Application No. 60/397,487 having a filing date of July 19, 2002, and, as discussed in the Appeal Brief, the pending claims are fully supported under 35 U.S.C. §112 by this provisional application. Accordingly, the captioned application has the same affect to the claimed inventions as though filed on the date of the provisional application, i.e., July 19, 2002. Cullen, et al. has a filing date of May 5, 2003. Thus, the Cullen, et al. publication is not prior art to the pending claims. Cullen, et al. claims filing benefit of a previously filed U.S. Provisional Application No. 60/377,224, having a filing date of May 3, 2002¹. Any rejection of the pending claims must be with reference to the provisional application of Cullen, et al.

The provisional application to which Cullen, et al. claims filing benefit is not identical to the Cullen, et al. published application. For instance, throughout the Examiner's Answer reference is made to paragraphs 0022 and 0023 of Cullen, et al. However, paragraph 0023 of the Cullen, et al. published application does not appear in the Cullen, et al. provisional application at all. Additionally, paragraph 0022 of the Cullen, et al. published application is not identical to the corresponding paragraph of the provisional application. In fact, not only is paragraph 0022 of the Cullen, et al. publication not identical to the corresponding paragraph of the provisional application, it

¹ By presentation of these arguments, Appellants in no way admit that the Cullen, et al. provisional application is proper prior art to the captioned application.

actually contains critical differences and is in conflict with the corresponding paragraph of the provisional application.

For instance, in the provisional application, it is stated that “[w]hile it is preferred that the stem comprise a perfectly complementary duplex (but for any 3’ tail), ‘bulges’ can be present.” However, in the published application Cullen, et al. states “[t]he stem can comprise a perfectly complementary duplex (but for any 3’ tail), however, ‘bulges’ can be present on either arm of the stem and may be preferred.” Thus, from the time of the provisional application to that of the published application, Cullen, et al. has completely altered what is considered to be the important (i.e., preferred) aspects of the disclosure. According to the provisional application, the stem preferably comprises a complementary duplex, which is in contrast to the requirements of the pending claims. Conversely to the provisional, the published Cullen, et al. application recognizes that bulges on the construct may be important.

Additionally, in the Cullen, et al. provisional application the paragraph corresponding to paragraph 0022 of the published application states, “[a]dvantageously, the entire miRNA-containing stem is complementary to the target sequence, even in regions of the stem 3’ and 5’ to the miRNA.” This sentence has been completely removed from the published application. This sentence is significant because if one were to apply this teaching to the modification of plant miRNA precursors, with their typically long stems, the resulting construct would be an RNAi construct. RNAi constructs have been well known to those of ordinary skill in the art for quite some time. RNAi constructs are recognized and sequentially processed to produce siRNA, rather than miRNA as is proposed in the published Cullen, et al. application. Thus, the

guidance provided by the Cullen, et al. provisional application would lead one of ordinary skill in the art to modify a plant miRNA precursor to produce an RNAi construct that would direct silencing of a target mRNA via the RNAi pathway rather than an artificial miRNA that would direct silencing via the miRNA pathway. The inclusion of this sentence in the provisional reiterates the other teachings of the provisional application that the disclosed constructs are designed in a different fashion and for a different purpose than are the constructs of the pending claims.

Appellants respectfully maintain that paragraphs 0022 and 0023 of the Cullen, et al. published application have been improperly relied upon in the rejection of the claims.

Additionally, Paragraphs 0024 and 0027, referred to at the bottom of page 9 of the Examiner's Answer, are not identical to the corresponding paragraphs of the Cullen, et al. provisional. Additional differences exist throughout the two applications as well. Appellants respectfully maintain that the rejections of the claims have been based upon a reference that is not proper prior art to the pending claims.

Appellants further maintain that the pending claims patentably define over the Cullen, et al. provisional application. For instance, the pending claims require that the exogenous miRNA sequence of the plant miRNA precursor maintains the length of the endogenous miRNA sequence which it replaces and also require that the nucleotides of the miRNA precursor opposite the exogenous section maintain the double strandedness and mismatches of the precursor. Throughout the Examiner's Answer it is admitted that Cullen, et al. does not teach this requirement of the claims. For instance, in the first full paragraph of page 10 of the Answer, it is stated:

"Appellant's argument is not persuasive to suggest that maintaining mismatches (bulges) present in an endogenous miRNA sequence, following replacement with an exogenous miRNA sequence in an artificial miRNA precursor construct is absolutely important for efficient miRNA processing from the artificial miRNA precursor. See for example figures 2-3 of Cullen, et al., ..."

Thus, the Answer accurately points out that Cullen, et al. does not maintain these required aspects of the pending claims, but is still able to form and process a nucleotide construct. The Examiner appears to be in agreement with the Appellant, i.e., according to the teachings of Cullen, et al., the length and mismatches of the miRNA precursor are not maintained when modifying the precursor with the exogenous miRNA sequence. However, the pending claims require these limitations.

This argument is repeated throughout the Examiner's Answer. See, e.g., page 13, the paragraph bridging pages 15 and 16, page 21 and page 22. For instance, at page 21 the Examiner states:

"It is also important to note that maintaining mismatches (bulges) present in an endogenous miRNA sequence, following replacement with an exogenous miRNA sequence in an artificial miRNA precursor construct is not important for maintaining stable secondary structure of miRNA precursor for efficient miRNA processing from the artificial miRNA precursor. This is evident from the teachings of Cullen, et al., ..."

Appellants respectfully submit that the question to be answered is not what the Examiner believes is or is not important in miRNA processing, but rather what is required by the pending claims and what is taught by the prior art with regard to those claim requirements. As noted by the Examiner, Cullen, et al. teaches that maintaining the length and mismatches of the original construct is not important (Examiner's Answer, p. 21, second full paragraph). However, this is required by the pending claims.

As argued in the Appeal Brief and pointed out throughout the Examiner's Answer, one of ordinary skill in the art, upon reading Cullen, et al., would understand

that maintaining the length and mismatches of the original construct is not important. As a result of this teaching, one of ordinary skill in the art would be led down a path that differs from that of the Appellants, in which the length and mismatches of the original miRNA precursor must be maintained upon replacement of the miRNA sequence with an exogenous miRNA sequence.

Appellants further point out that while these elements of the claims are absolutely important to the pending claims, in that they are required by the claims, the Appellant is not implying that the Cullen, et al. reference is therefore disclosing a nonworking invention. However, as previously discussed, when the teachings of the Cullen provisional patent are applied to plant miRNA precursors, the result is an RNAi construct, not a construct that would produce an artificial miRNA. It is the contention of the Appellant that through the maintenance of the length and mismatches of the original miRNA precursor in forming the new miRNA precursor that includes the exogenous miRNA sequence in the context of the original endogenous miRNA precursor structure, the processing of the construct occurs naturally through the miRNA pathway rather than through the RNAi pathway.

In self-contradiction to the statements of the Examiner's Answer outlined above, the Examiner's Answer also states that it would be obvious to maintain the length and mismatches of an endogenous miRNA precursor because it was unknown what the effect of removing the secondary structure would be and it would have been obvious to not alter it. However, and as pointed out throughout the Examiner's Answer, Cullen, et al. does alter the secondary structure and still is able to process the construct. The Examiner's Answer attempts to argue both 1) Cullen, et al. does not maintain the

secondary structure of the endogenous construct and still forms a processable modified construct and therefore the differences between the pending claims and Cullen, et al. teachings are not important and 2) one of skill in the art would not know what the effect of removing the secondary structure would be and therefore it is obvious that the secondary structure must be maintained when forming a modified construct. These arguments are contradictory to one another and fail to support a *prima facie* rejection under 35 U.S.C. §103.

The question remains, where, absent the teaching of the captioned application, is any teaching to suggest the maintenance of the length and mismatch structure of the miRNA precursor? Cullen, et al. teaches that bulges can exist on a stem (p. 7, ll. 2-4, Provisional application), but Cullen, et al. does not teach that the length and mismatches of the endogenous miRNA sequence must be maintained in the new construct that includes an exogenous miRNA sequence, as is required by the claims. In fact, given the fact that Cullen, et al. alters both the length and mismatches of a construct in the examples of the application and presents these alterations as the "preferred" structure in the provisional application, Appellants maintain that one of skill in the art, given the teachings of Cullen, et al., would understand that maintaining the length and mismatches is simply not necessary nor important. Yet these elements are required by the pending claims.

At page 12 of the Examiner's Answer, it was suggested that the Appellants have mischaracterized the teachings of Cullen, et al. by suggesting that Cullen, et al. teaches that a stable secondary structure is unimportant. Appellants disagree. What Appellants suggest is that Cullen, et al. teaches that maintaining the length and mismatches of the

miRNA precursor is not important and, as discussed above, the Examiner's Answer agrees with this understanding. This is further evidenced by the fact that Cullen, et al. never mentions the desirability of such and in the examples fails to maintain either the length or mismatches of an endogenous precursor when forming a new construct with an exogenous miRNA sequence. Not only is the desirability of maintaining either the length or the mismatches not mentioned in the Cullen, et al. provisional application, the application points to alterations in the length and the mismatch structure of the modified miRNA precursor as being "preferred" and "advantageous". Cullen, et al. simply does not maintain the length or mismatches of the original miRNA precursor.

As correctly pointed out by the Examiner at page 22 of the Examiner's Answer, it is understood that a stable secondary structure is essential for efficient processing of an miRNA precursor to release miRNA. The pending claims of the captioned application rely upon and require the maintenance of the secondary structure of the endogenous miRNA precursor to provide efficient processing through the natural miRNA pathway. However, neither Cullen, et al. nor any of the other cited references teach a method of developing a miRNA precursor that uses the secondary structure of an endogenous miRNA precursor to provide that necessary stability according to the methods of the pending claims. Specifically, neither Cullen, et al. nor any of the other cited references disclose or suggest a plant, a plant cell or a seed in which an endogenous miRNA sequence has been replaced with an exogenous miRNA sequence that maintains the length of the endogenous sequence and also in which the nucleotides opposite the exogenous sequence have been modified to maintain double strandedness and

mismatches within the context of an endogenous miRNA precursor, as is required in the pending claims.

In conclusion, Appellants request favorable action and allowance of the presently pending claims.

Respectfully requested,

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Date: 6/16/10



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